DEPARTMENT OF BACTERIOLOGY,
ST. THOMAS'S HOSPITAL MEDICAL SCHOOL,
LONDON, S.E.1.

PROFESSOR RONALD HARE.

TELE: WATERLOO 5656 (EX. 52).

Meynell

15th December 1958.

Professor J. Lederberg,
Department of Genetics,
University of Wisconsin,
Madison 6,
WISCONSIN.

Dear Josh,

Thank you very much for your letter and for remembering my problem when you must have had a great deal to do. It would be fascinating to carry out this experiment by density gradient centrigugation but although it would clearly give the answer if cells divided but were not killed, I am not sure what would occur when division and killing took place at the same time. If half the labelled cells died in the 1st generation, one might have a reserve of fully labelled dead cells that would persist, act like live cells during the assay and so upset the estimates. This reserve might be increased by ½-hot pairs (or cells) for the 2nd generation and so on. One might be able to exclude this if the viable count was proportional to N content of the bands. If this was not found, a way round the difficulty would be to separate live bacteria from dead bacteria + mouse cells and then measure the mean isotope content per live cell. I actually tried this once using a P32 labelled motile Salmonella which I hoped to separate by implanting the organ homogenate in one part of a plate of semi solid agar and harvesting the live cells from the rest of the plate after incubation. I stopped soon after I had started when Monod's paper on turnover of DNA-P in stationary phase B. Coli appeared. I don't know if N^{15} is conserved regardless of the growth state of the cells.

The superinfecting phage experiments are not going too badly. After superinfection at multiplicities >4, a marked fraction of superinfected cells die after in dilution in fresh medium and this has to be looked at. K12 ($\lambda h^{+} b$) is rapidly killed inside mice for only

1/10,000 of the inoculum survives 6 hours after infection but this persists for 72 hours at least. At the moment, the efficiency of induction is usually too low and this will have to be improved to get larger numbers of plaques. The low viable counts do at least bring out the sensitivity of the method although they are rather a hindrance.

Enclosed are some reprints showing where we have got to so far. Theinfection model can be done far more mathematically. A pupil of Neymans has had one attempt; however, the sums turned out to be so intractable that they gave him his Ph.D. for getting the distribution of times to death for mice each given one organism, it being assumed that death occurred when a mouse contained two organisms!

Bruce will have told you that, in the end, it was arranged that we should not go to Yale in January. You can imagine that our feelings are very mixed. We were sorry to hear that you had such an interrrupted journey to Stockholm and not to meet you; but perhaps you will be here again next summer.

With best wishes from us both for Christmas and the New Year,

Yours sincerely,

Guy.